From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

PHARMACIA & UPJOHN S.P.A. Via le Pasteur, 10 I-20014 Nerviano ITALIE

Date of mailing (day/month/year) 13 March 2000 (13.03.00)	
Applicant's or agent's file reference FC 861/5	IMPORTANT NOTIFICATION
International application No.	International filing date (day/month/year)
PCT/EP00/00745	31 January 2000 (31.01.00)
International publication date (day/month/year)	Priority date (day/month/year)
Not yet published	25 February 1999 (25.02.99)
Applicant	
PHARMACIA & UPJOHN S.P.A. et al	

- 1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- 2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
- 3. An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- 4. The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
25 Febr 1999 (25.02.99)	9904387.9	GB	01 Marc 2000 (01.03.00)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer

S. De Michiel

Telephone No. (41-22) 338.83.38

Facsimile No. (41-22) 740.14.35

M PCT

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

From the INTERNATIONAL BUREAU

PHARMACIA & UPJOHN S.P.A.

Viale Pasteur, 10 I-20014 Nerviano ITALIE

1) Nopub 2) Love chih pronitye prisignation

Date of mailing (day/month/year)

31 August 2000 (31.08.00)

Applicant's or agent's file reference

FC 861/5

IMPORTANT NOTICE

International application No. PCT/EP00/00745

International filing date (day/month/year)

31 January 2000 (31.01.00)

Priority date (day/month/year)
25 February 1999 (25.02.99)

Applicant

PHARMACIA & UPJOHN S.P.A. et al

 Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice: AU,KP,KR,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AE,AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,CA,CH,CN,CR,CU,CZ,DE,DK,DM,EA,EE,EP,ES,FI,GB,GD,GE,GH,GM,HR,HU,ID,IL,IN,IS,JP,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MA,MD,MG,MK,MN,MW,MX,NO,NZ,OA,PL,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,TZ,UA,UG,UZ,VN,YU,ZA,ZW The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 31 August 2000 (31.08.00) under No. WO 00/50032

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the **national phase**, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Authorized officer

J. Zahra

Telephone No. (41-22) 338.83.38

Facsimile No. (41-22) 740.14.35

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)
23 October 2000 (23.10.00)

International application No.
PCT/EP00/00745

International filing date (day/month/year)
31 January 2000 (31.01.00)

in its capacity as elected Office

Applicant's or agent's file reference
FC 861/5

Priority date (day/month/year)
25 February 1999 (25.02.99)

Applicant

GERONI, Cristina et al

1.	The designated Office is hereby notified of its election made:
••	<u></u>
	X in the demand filed with the International Preliminary Examining Authority on:
	15 September 2000 (15.09.00)
	in a notice effecting later election filed with the International Bureau on:
2.	The election X was
	was not
	made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Authorized officer

R. E. Stoffel

Telephone No.: (41-22) 338.83.38

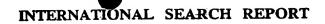
Facsimile No.: (41-22) 740.14.35



Inte. Jonal Application No

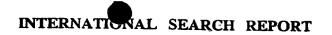
		PCT/EP	00/00745
	IFICATION OF SUBJECT MATTER A61K31/396 A61K31/351 A61P35/(//(A61K31/396,31:352),(A61K31/396 (A61K31/351,31:351) International Patent Classification (IPC) or to both national classific	,31:351),(A61K31/352,	31:351),
	SEARCHED	amon and IPC	
	ocumentation searched (classification system followed by classification	on symbols)	
	tion searched other than minimum documentation to the extent that s		
Electronic d	lata base consulted during the international search (name of data ba	se and, where practical, search terms u	ped)
C. DOCUM	ENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the rel	evant passages	Relevant to claim No.
P,X	WO 99 48503 A (CARUSO MICHELE ;GERONI CRISTINA (IT); PHARMACIA & UPJOHN SPA (IT);) 30 September 1999 (1999-09-30) claims 1-7		1-9
Y	EDER JP ET AL: "Sequence effect irinotecan (CPT-11) and topoisome inhibitors in vivo" CANCER CHEMOTHERAPY AND PHARMACOLOGY, DE, SPRINGER VERLAG, vol. 42, no. 4, 1998, pages 327-3 XP002112007 ISSN: 0344-5704 abstract page 334	erase II BERLIN.	1-9
	ner documents are listed in the continuation of box C.	Patent family members are list	ed in annex.
A document defining the general state of the art which is not considered to be of particular relevance *E* earlier document but published on or after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention filing date *L* document which may throw doubte on priority claim(e) or which is cited to establish the publication date of another citation or other special reason (as specified) *O* document referring to an oral disclosure, use, exhibition or other means *P* document published prior to the international filing date but later than the priority date claimed *It is document of particular relevance; the claimed invention cannot be considered novel or cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone cannot be considered to Involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person sidiled in the art. **C** document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention *X** document of particular relevance; the claimed invention involve an inventive step when the document is taken alone to cannot be considered to Involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person sidiled in the art.			th the application but theory underlying the eclaimed invention not be considered to document is taken alone eclaimed invention inventive step when the more other such document on a person skilled at temily
	2 May 2000	Date of mailing of the international:	подел пород
Name and m	nailing address of the ISA European Patent Office, P.B. 5818 Patentiaan 2 NL – 2280 HV Rijawijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,	Authorized officer Herrera, S	
	Fax: (+31-70) 340-3016	Herrera, J	

1



Ints Jonal Application No PCT/EP 00/00745

0.00==	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	PCI/EP 00/	
Category *			lelevant to claim No.
Y	US 5 532 218 A (BARGIOTTI ALBERTO ET AL) 2 July 1996 (1996-07-02) cited in the application claims 1,6,10	·	1-9
Y	cited in the application claims 1,6,10 US 5 496 808 A (BARGIOTTI ALBERTO ET AL) 5 March 1996 (1996-03-05) cited in the application claims 1,2,29		1-9
			•



information on patent family members

Inte. Jonal Application No PCT/EP 00/00745

	in search report		date		member(s)	date
WO	9948503	A	30-09-1999	AU	3331499 A	18-10-1999
US	5532218	Α	02-07-1996	AT	157369 T	15-09-1997
				AU	676625 B	13-03-1997
				AU	1066095 A	03-07-1995
				CA	2154890 A	22-06-1995
				CN	1117734 A,B	28-02-1996
				DE	69405214 D	02-10-1997
				DE	69405214 T	29-01-1998
				DK	683788 T	27-10-1997
				₩O	9516695 A	22-06-1995
				EP	0683788 A	29-11-1995
				ES	2107294 T	16-11-1997
				FI	953784 A	09-08-1995
				GR	3025266 T	27-02-1998
				HU IL	73172 A	28-06-1996
				JP	111725 A 8506835 T	15-07-1998
				NO	8506835 T 953163 A	23-07-1996
				NZ NZ	276401 A	02-10-1995
				PL	310177 A	24-10-1997 27-11-1995
				ZA	9409701 A	12-12-1995
						12-12-1995
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				AU	661012 B	13-07-1995
				AU	2229492 A	11-02-1993
				CA	2112818 A	21-01-1993
				CN	1069981 A,B	17-03-1993
				CZ	9400024 A	13-07-1994
				DE	69208400 D	28-03-1996
				DE	69208400 T	27-06-1996
				DK	521458 T	18-03-1996
				WO EP	9301201 A 0521458 A	21-01-1993
				FI	940011 A	07-01-1993
				GR	3019429 T	03-01-1994 30-06-1996
				HK	1006460 A	26-02-1999
				HU	70480 A	20-02-1999 30-10-1995
				IE	76921 B	05-11-1995 05-11-1997
				IL	102409 A	08-12-1995
				ĴP	6508841 T	06-12-1995
				MX	9203928 A	01-04-1993
				NO	940026 A	16-02-1994
				NZ	243450 A	25-11-1993
				ZA	9204971 A	31-03-1993



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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's	or agent's file reference		See Notification of Transmittal of International
FC 861/5		FOR FURTHER ACTION	Preliminary Examination Report (Form PCT/IPEA/416)
Internationa	l application No.	International filing date (day/month	/year) Priority date (day/month/year)
PCT/EP0	0/00745	31/01/2000	25/02/1999
Internationa A61K31/3	l Patent Classification (IPC) or na 396	tional classification and IPC	
PHARMA	CIA & UPJOHN S.P.A.		
	nternational preliminary exami transmitted to the applicant a		by this International Preliminary Examining Authority
2. This F	EPORT consists of a total of	4 sheets, including this cover sl	neet.
b∈	een amended and are the bas		e description, claims and/or drawings which have ontaining rectifications made before this Authority ons under the PCT).
These	annexes consist of a total of	sheets.	
3. This re	eport contains indications rela	ting to the following items:	
ı	☑ Basis of the report		
11	☐ Priority		
111	☐ Non-establishment of o	pinion with regard to novelty, inv	entive step and industrial applicability
IV	☐ Lack of unity of invention	n	
٧	Reasoned statement ur citations and explanatio	nder Article 35(2) with regard to r	novelty, inventive step or industrial applicability;
VI	☐ Certain documents cite	ed	
VII	☐ Certain defects in the in	(**)	
VIII	☐ Certain observations on	the international application	
Date of subn	nission of the demand	Date of c	ompletion of this report
15/09/200	0	29.05.20	01
	nailing address of the international examining authority: European Patent Office		Superior Control of the Control of t
<i>)</i>)))	D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656	Herrera	a, S
	Fax: +49 89 2399 - 4465	•	De No. +49.89.2399.8464

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/00745

I. Basis	of the	report
----------	--------	--------

1.	the and	receiving Office in	nents of the international application (Replacement sheets which have been furnished to response to an invitation under Article 14 are referred to in this report as "originally filed" of this report since they do not contain amendments (Rules 70.16 and 70.17)):
	1-6		as originally filed
	Cla	ims, No.:	
	1-9		as originally filed
2.			juage, all the elements marked above were available or furnished to this Authority in the international application was filed, unless otherwise indicated under this item.
	The	ese elements were a	available or furnished to this Authority in the following language: , which is:
		the language of a	translation furnished for the purposes of the international search (under Rule 23.1(b)).
		the language of pu	ublication of the international application (under Rule 48.3(b)).
		the language of a 55.2 and/or 55.3).	translation furnished for the purposes of international preliminary examination (under Rule
3.			eleotide and/or amino acid sequence disclosed in the international application, the y examination was carried out on the basis of the sequence listing:
		contained in the in	ternational application in written form.
		filed together with	the international application in computer readable form.
		furnished subsequ	ently to this Authority in written form.
		furnished subsequ	ently to this Authority in computer readable form.
			t the subsequently furnished written sequence listing does not go beyond the disclosure in oplication as filed has been furnished.
		The statement that listing has been fu	t the information recorded in computer readable form is identical to the written sequence rnished.
4.	The	amendments have	resulted in the cancellation of:
		the description,	pages:
		the claims,	Nos.:
		the drawings,	sheets:
5.			en established as if (some of) the amendments had not been made, since they have beer eyond the disclosure as filed (Rule 70.2(c)):

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/00745

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

- 6. Additional observations, if necessary:
- V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- 1. Statement

Novelty (N) Yes: Claims 1-9

No: Claims

Inventive step (IS) Yes: Claims

No: Claims 1-9

Industrial applicability (IA) Yes: Claims 1-6 No: Claims

2. Citations and explanations see separate sheet

Section V

- 1. Reference is made to the following documents:
 - D1: US-A-5 532 218 (BARGIOTTI ALBERTO ET AL) 2 July 1996 (1996-07-02)
 - D2: US-A-5 496 808 (BARGIOTTI ALBERTO ET AL) 5 March 1996 (1996-03-05)
 - D3: EDER JP ET AL: 'Sequence effect of irinotecan (CPT-11) and topoisomerase II inhibitors in vivo' CANCER CHEMOTHERAPY AND PHARMACOLOGY, DE, SPRINGER VERLAG, BERLIN, vol. 42, no. 4, 1998, pages 327-335,
- 2. The subject-matter of the present claims appears to be novel over the prior art. since products comprising the two required elements have not been disclosed before (Art 33(2) PCT).
- 3. The used anthracyclines are however known from D1 and D2 as antineoplastic agents. It is further suggested in D3 to combine antineoplastic agent with inhibitors of topoisomerase and that this combination would have a synergistic activity. For the skilled person it appears to be obvious to combine the teachings of D1 or D2 with D3 and arrive at the subject-matter of the present claims, i.e. the requirements of Article 33 (3) PCT have not been fulfilled. It is pointed out that not even a synergistic effect can provide evidence for an inventive step, since this effect has been suggested in D3.
- For the assessment of the present claims 7-9 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.



PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference		f Transmittal of International Search Report		
FC 861/5 (Form PCT/ISA/220) as well as, where applicable, item 5 below.				
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)		
PCT/EP 00/00745	31/01/2000	25/02/1999		
Applicant				
PHARMACIA & UPJOHN S.P.A.				
This International Search Report has bee according to Article 18. A copy is being tra	n prepared by this International Searching Auth ansmitted to the International Bureau.	nority and is transmitted to the applicant		
This International Search Report consists It is also accompanied by	of a total of sheets. a copy of each prior art document cited in this	report.		
Basis of the report				
	international search was carried out on the bas ess otherwise indicated under this item:	sis of the international application in the		
the international search w Authority (Rule 23.1(b)).	as carried out on the basis of a translation of the	ne international application furnished to this		
was carried out on the basis of the		ternational application, the international search		
	rnational application in computer readable form	n.		
furnished subsequently to this Authority in written form.				
furnished subsequently to this Authority in computer readble form. the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the				
	s filed has been furnished.	bes not go beyond the disclosure in the		
the statement that the info furnished	the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished			
2. Certain claims were fou	nd unsearchable (See Box I).			
3. Unity of invention is lac	king (see Box II).	•		
4. With regard to the title ,				
X the text is approved as su	bmitted by the applicant.			
the text has been establis	the text has been established by this Authority to read as follows:			
5. With regard to the abstract,				
X the text is approved as su	bmitted by the applicant.			
the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.				
6. The figure of the drawings to be publ	ished with the abstract is Figure No.	<u> </u>		
as suggested by the appli	cant.	None of the figures.		
because the applicant fail	ed to suggest a figure.			
because this figure better	characterizes the invention.			

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) $IPC\ 7\ A61K\ A61P$

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

	the relevant passages	Relevant to claim No.
Category °	Citation of document, with indication, where appropriate, of the relevant passages	
Р,Х	WO 99 48503 A (CARUSO MICHELE ;GERONI CRISTINA (IT); PHARMACIA & UPJOHN SPA (IT);) 30 September 1999 (1999-09-30) claims 1-7	1-9
Y	EDER JP ET AL: "Sequence effect of irinotecan (CPT-11) and topoisomerase II inhibitors in vivo" CANCER CHEMOTHERAPY AND PHARMACOLOGY, DE, SPRINGER VERLAG, BERLIN, vol. 42, no. 4, 1998, pages 327-335, XP002112007 ISSN: 0344-5704 abstract page 334	1-9

Y Further documents are listed in the continuation of box C.	X Patent family members are listed in annex.
 Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filling date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed 	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
Date of the actual completion of the international search	Date of mailing of the international search report
12 May 2000	22/05/2000
Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Herrera, S



ernational Application No PCT/EP 00/00745

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
<u> </u>		
	US 5 532 218 A (BARGIOTTI ALBERTO ET AL) 2 July 1996 (1996-07-02) cited in the application claims 1,6,10	1-9
	US 5 496 808 A (BARGIOTTI ALBERTO ET AL) 5 March 1996 (1996-03-05) cited in the application claims 1,2,29	1-9
	,	
	,	

Information on patent family members

PCT/EP 00/00745

cited in search repo	rt 	Publication date		Patent family member(s)		Publication date
พื้อ: 9948503	Α	30-09-1999	AU	3331499	Α	18-10-1999
US 5532218	Α	02-07-1996	AT	157369	T	15-09-1997
			AU	676625	В	13-03-1997
			AU	1066095	Α	03-07-1995
			CA	2154890		22-06-1995
			CN	1117734		28-02-1996
			DE	69405214	D	02-10-1997
			DE		T	29-01-1998
			DK	683788		27-10-1997
•			WO	9516695		22-06-1995
			EP	0683788	Α	29-11-1995
			ES	2107294	T	16-11-1997
			FI	953784	Α	09-08-1995
			GR	3025266	Ţ	27-02-1998
			HU	73172		28-06-1996
			IL	111725		15-07-1998
			JP		T	23-07-1996
			NO NZ	953163		02-10-1995
			NZ	276401		24-10-1997
			PL ZA	310177 9409701		27-11-1995 12-12-1995
US 5496808	Α	05-03-1996	AT	. 134376	 Т	15-03-1996
*			AU	661012		13-07-1995
			AU CA	222 94 92 2112818		11-02-1993 21-01-1993
			CN	1069981		17-03-1993
			CZ	9400024		13-07-1994
		•	DE	69208400		28-03-1996
			DE		T	27-06-1996
			DK	521458	Ť	18-03-1996
			WO	9301201		21-01-1993
			EP	0521458		07-01-1993
			FI	940011		03-01-1994
			GR	3019429	T	30-06-1996
			HK	1006460		26-02-1999
			HU	70480		30-10-1995
			IE,	76921		05-11-1997
			IL	102409		08-12-1995
			JP	6508841		06-10-1994
			MX	9203928		01-04-1993
			NO	940026		16-02-1994
			NZ ZA	243450 9204971		25-11-1993 31-03-1993
				020707	/1	31-03-1003

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REC'D	3	1	MAY	2001	
WIPO			F	CT	١

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applic	cant's c	r age	nt's file reference	FOR EURTHER ACTION		fication of Transmittal of International		
FC 8	361/5			FOR FURTHER ACTION	Prelimina	ary Examination Report (Form PCT/IPEA/416)		
Intern	ational	appli	cation No.	International filing date (day/mont	h/year)	Priority date (day/month/year)		
PCT	/EP0	0/00	745	31/01/2000		25/02/1999		
	national K31/3		nt Classification (IPC) or na	tional classification and IPC				
Applio PHA		CIA	& UPJOHN S.P.A.					
			ational preliminary exam smitted to the applicant a		d by this Ir	ternational Preliminary Examining Authority		
2.	This R	EPO	RT consists of a total of	4 sheets, including this cover s	sheet.			
	be (s	en a ee R	mended and are the bas	sis for this report and/or sheets 07 of the Administrative Instruct	containing	ion, claims and/or drawings which have rectifications made before this Authority the PCT).		
3.	This re	eport	contains indications rela	ating to the following items:				
	П		Priority					
	Ш		Non-establishment of o	ppinion with regard to novelty, ir	ventive ste	ep and industrial applicability		
	IV		Lack of unity of invention					
	V	⊠	Reasoned statement u citations and explanation	nder Article 35(2) with regard to ons suporting such statement	novelty, ir	ventive step or industrial applicability;		
	VI							
	VII		Certain defects in the i	nternational application				
	VIII		Certain observations o	n the international application				
Date	of sub	missio	on of the demand	Date o	f completion	of this report		
15/0	9/200	00		29.05	2001			
		exam	g address of the international ining authority: opean Patent Office	al Author	ized officer	E MICHES MICHES		
	<i>9</i>))	D-80	0298 Munich +49 89 2399 - 0 Tx: 52365		Herrera, S			
l —			+49 89 2399 - 4465	•		1 90 2200 8464		

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/00745

I. Basis of the report

1	the an	With regard to the elements of the international application (Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)): Description , pages:							
	1-6	6	as originally filed						
	Cla	aims, No.:							
	1-9)	as originally filed						
2	Wi	th regard to the land	Ulago, all the elements marked characters and lable as forcished as the U.S. A. U.S. S. U.S.						
۷.	lan	guage in which the i	uage, all the elements marked above were available or furnished to this Authority in the nternational application was filed, unless otherwise indicated under this item.						
	The	ese elements were a	vailable or furnished to this Authority in the following language: , which is:						
		the language of a t	ranslation furnished for the purposes of the international search (under Rule 23.1(b)).						
		the language of pu	blication of the international application (under Rule 48.3(b)).						
		the language of a t 55.2 and/or 55.3).	ranslation furnished for the purposes of international preliminary examination (under Rule						
3.	Wit inte	h regard to any nuc ernational preliminary	leotide and/or amino acid sequence disclosed in the international application, the examination was carried out on the basis of the sequence listing:						
		contained in the int	ernational application in written form.						
		filed together with t	he international application in computer readable form.						
		furnished subseque	ently to this Authority in written form.						
		☐ furnished subsequently to this Authority in computer readable form.							
		The statement that the international ap	the subsequently furnished written sequence listing does not go beyond the disclosure in plication as filed has been furnished.						
		The statement that listing has been fur	the information recorded in computer readable form is identical to the written sequence nished.						
4.	The	amendments have	resulted in the cancellation of:						
		the description,	pages:						
		the claims,	Nos.:						
		the drawings,	sheets:						
5.		This report has bee considered to go be	n established as if (some of) the amendments had not been made, since they have been eyond the disclosure as filed (Rule 70.2(c)):						



International application No. PCT/EP00/00745

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

- 6. Additional observations, if necessary:
- V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- 1. Statement

Novelty (N)

Yes: No: Claims 1-9 Claims

Inventive step (IS)

Yes:

Claims

No:

Claims 1-9

Industrial applicability (IA)

Yes:

Claims 1-6

No: Claims

2. Citations and explanations see separate sheet

Section V

- 1. Reference is made to the following documents:
 - D1: US-A-5 532 218 (BARGIOTTI ALBERTO ET AL) 2 July 1996 (1996-07-02)
 - D2: US-A-5 496 808 (BARGIOTTI ALBERTO ET AL) 5 March 1996 (1996-03-05)
 - D3: EDER JP ET AL: 'Sequence effect of irinotecan (CPT-11) and topoisomerase II inhibitors in vivo' CANCER CHEMOTHERAPY AND PHARMACOLOGY, DE, SPRINGER VERLAG, BERLIN, vol. 42, no. 4, 1998, pages 327-335,
- 2. The subject-matter of the present claims appears to be novel over the prior art, since products comprising the two required elements have not been disclosed before (Art 33(2) PCT).
- 3. The used anthracyclines are however known from D1 and D2 as antineoplastic agents. It is further suggested in D3 to combine antineoplastic agent with inhibitors of topoisomerase and that this combination would have a synergistic activity. For the skilled person it appears to be obvious to combine the teachings of D1 or D2 with D3 and arrive at the subject-matter of the present claims, i.e. the requirements of Article 33 (3) PCT have not been fulfilled. It is pointed out that not even a synergistic effect can provide evidence for an inventive step, since this effect has been suggested in D3.
- 4. For the assessment of the present claims 7-9 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

•			P 00/00745		
· ·	ification of subject matter A61K31/396 A61K31/351 A61P35/ //(A61K31/396,31:352),(A61K31/396 (A61K31/351,31:351)	3,31:351),(A61K31/35	2,31:351),		
	o International Patent Classification (IPC) or to both national classification	cation and IPC			
	SEARCHED commentation searched (classification system followed by classification system followed system followed by classification system followed	tion symbols)			
IPC 7	A61K A61P				
Documentar	tion searched other than minimum documentation to the extent that	such documents are included in the	ields searched		
Electronic d	lata base consulted during the international search (name of data b	ase and, where practical, search term	rs used)		
C. DOCUM	ENTS CONSIDERED TO BE RELEVANT		S. L. Lands No.		
Category *	Citation of document, with indication, where appropriate, of the re	evant passages	Relevant to claim No.		
P,X	WO 99 48503 A (CARUSO MICHELE ;G CRISTINA (IT); PHARMACIA & UPJOH (IT);) 30 September 1999 (1999-0 claims 1-7	1-9			
Υ	EDER JP ET AL: "Sequence effect irinotecan (CPT-11) and topoisom inhibitors in vivo" CANCER CHEMOTHERAPY AND PHARMACOLOGY, DE, SPRINGER VERLAG, vol. 42, no. 4, 1998, pages 327-XP002112007 ISSN: 0344-5704 abstract page 334	erase II BERLIN,	1-9		
X Furth	ner documents are listed in the continuation of box C.	Patent family members are	e listed in annex.		
A docume conside filing de "L* documer which is citation of the ritation other in "P* documer "P* do	nt which may throw doubts on priority claim(s) or is cited to establish the publication date of another is or other special reason (as specified) ent referring to an oral diaclosure, use, exhibition or	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to Involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family			
Date of the a	actual completion of the International search	Date of mailing of the internation	inal search report		
12	2 May 2000	22/05/2000			
Name and m	nailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Authorized officer Herrera, S			

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ints Jonal Application No PCT/EP 00/00745

Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT Category * Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No.						
	US 5 532 218 A (BARGIOTTI ALBERTO ET AL 2 July 1996 (1996-07-02) cited in the application claims 1,6,10	1-9				
	US 5 496 808 A (BARGIOTTI ALBERTO ET AL 5 March 1996 (1996-03-05) cited in the application claims 1,2,29	1-9				
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information on patent family members

inte. Jonal Application No PCT/EP 00/00745

· c	Patent document ted in search report		Publication date		Patent family member(s)	Publication date
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